APR 2 9 2302

SEQUENCE LISTING

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<120> HUMAN KCR1 REGULATION OF HERG POTASSIUM CHANNEL BLOCK

<130> 1242-49-2

<140> US/10/000,151

<141> 2001-10-30

<150> 60/244,340

<151> 2000-10-30

<160> 7

<170> PatentIn version 3.0

<210> 1

<211> 1857

<212> DNA

<213> Homo sapiens

<220>

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1 5 10 15

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96

Phe Leu Val Ser Cys Leu Leu Phe Ser Ala Phe Ser Arg Ala Leu Arg

20 25 30

gag ccc tac atg gac gag atc ttc cac ctg cct cag gcg cag cgc tac

Glu Pro Tyr Met Asp Glu Ile Phe His Leu Pro Gln Ala Gln Arg Tyr tgt gag ggc cat ttc tcc ctt tcc cag tgg gat ccc atg att act aca Cys Glu Gly His Phe Ser Leu Ser Gln Trp Asp Pro Met Ile Thr Thr tta cet gge ttg tae etg gtg tea gtt gga gtg gte aaa eet gee att Leu Pro Gly Leu Tyr Leu Val Ser Val Gly Val Val Lys Pro Ala Ile tgg atc ttt gga tgg tct gaa cat gtt gtc tgc tcc att ggg atg ctc Trp Ile Phe Gly Trp Ser Glu His Val Val Cys Ser Ile Gly Met Leu aga ttt gtt aat ctt ctc ttc agt gtt ggc aac ttc tat tta cta tat Arg Phe Val Asn Leu Leu Phe Ser Val Gly Asn Phe Tyr Leu Leu Tyr ttg ctt ttc cac aag gta caa ccc aga aac aag gct gcc tca agt atc Leu Leu Phe His Lys Val Gln Pro Arq Asn Lys Ala Ala Ser Ser Ile cag aga gtc ttg tca aca tta aca cta gca gta ttt cca aca ctt tat Gln Arq Val Leu Ser Thr Leu Thr Leu Ala Val Phe Pro Thr Leu Tyr

| ttt tt 480 Phe Ph | | | | | | | | | | | | | | |
|-------------------------|-------|-----|-----|-----|-----|------|-----|-----|-----|-----|------|------|-----|-----|
| 145 | ZADII | THE | БСС | 150 | 171 | 1111 | Gru | AIG | 155 | DCI | rice | 1110 | THE | 160 |
| ctt tt | gca | tat | ttg | atg | tgt | ctt | tat | gga | aat | cat | aaa | act | tca | gcc |
| Leu Ph | e Ala | Tyr | Leu | Met | Cys | Leu | Tyr | Gly | Asn | His | Lys | Thr | Ser | Ala |
| | | | 165 | | | | | 170 | | | | | 175 | |
| ttc ct | gga | ttt | tgt | ggc | ttc | atg | ttt | cgg | caa | aca | aat | atc | atc | tgg |
| Phe Le | ı Gly | Phe | Cys | Gly | Phe | Met | Phe | Arg | Gln | Thr | Asn | Ile | Ile | Trp |
| | | 180 | | | | | 185 | | | | | 190 | | |
| gct gt | c ttc | tgt | gca | aaa | aat | gtc | att | gca | caa | aag | tta | act | gag | gct |
| Ala Va | l Phe | Cys | Ala | Gly | Asn | Val | Ile | Ala | Gln | Lys | Leu | Thr | Glu | Ala |
| | 195 | | | | · | 200 | | | | | 205 | | | |
| tgg aaa | a act | gag | cta | caa | aag | aag | gaa | gac | aga | ctt | cca | cct | att | aaa |
| Trp Ly | s Thr | Glu | Leu | Gln | Lys | Lys | Glu | Asp | Arg | Leu | Pro | Pro | Ile | Lys |
| 21 |) | | | | 215 | | | | | 220 | | | | |
| gga cca 720 | a ttt | gca | gaa | ttc | aga | aaa | att | ctt | cag | ttt | ctt | ttg | gct | tat |
| Gly Pro | o Phe | Ala | Glu | Phe | Arg | Lys | Ile | Leu | Gln | Phe | Leu | Leu | Ala | Tyr |
| 225 | | | | 230 | | | | | 235 | | | | | 240 |
| tcc ato | g tcc | ttt | aaa | aac | ttg | agt | atg | ctt | ttc | tgt | ttg | act | tgg | ccc |
| Ser Me | Ser | Phe | Lys | Asn | Leu | Ser | Met | Leu | Phe | Cys | Leu | Thr | Trp | Pro |
| | | | 245 | | | | | 250 | | | | | 255 | |

. ?

tac atc ctt ctg gga ttt ctg ttt tgt gct ttt gta gta gtt aat ggt Tyr Ile Leu Leu Gly Phe Leu Phe Cys Ala Phe Val Val Asn Gly gga att gtt att ggc gat cgg agt agt cat gaa gcc tgt ctt cat ttt Gly Ile Val Ile Gly Asp Arg Ser Ser His Glu Ala Cys Leu His Phe Pro Gln Leu Phe Tyr Phe Phe Ser Phe Thr Leu Phe Phe Ser Phe Pro cat ctc ctq tct cct aqc aaa att aag act ttt ctt tcc tta gtt tgg His Leu Leu Ser Pro Ser Lys Ile Lys Thr Phe Leu Ser Leu Val Trp aaa cat gga att ctg ttt ttg gtg gtt acc tta gtc tct gtg ttt tta Lys His Gly Ile Leu Phe Leu Val Val Thr Leu Val Ser Val Phe Leu gtt tgg aaa ttc act tat gct cat aaa tac ttg cta gca gac aat aga Val Trp Lys Phe Thr Tyr Ala His Lys Tyr Leu Leu Ala Asp Asn Arg cat tat act ttc tat gtg tgg aaa aga gtt ttt caa aga tat gca att His Tyr Thr Phe Tyr Val Trp Lys Arg Val Phe Gln Arg Tyr Ala Ile

ctg aaa tat ttg tta gtt cca gcc tat ata ttt gct ggt tgg agt ata 1152
Leu Lys Tyr Leu Leu Val Pro Ala Tyr Ile Phe Ala Gly Trp Ser Ile
370 375 380

gct gac tca ttg aaa tca aag cca att ttt tgg aat tta atg ttt ttc
1200
Ala Asp Ser Leu Lys Ser Lys Pro Ile Phe Trp Asn Leu Met Phe Phe
385
390
395
400

ata tgc ttg ttc att gtt ata gtt cct cag aaa ctg ctg gaa ttt cgt
1248
Ile Cys Leu Phe Ile Val Ile Val Pro Gln Lys Leu Leu Glu Phe Arg
405
410
415

tac ttc att tta cct tat gtc att tat agg ctt aac ata act ctg cct 1296

Tyr Phe Ile Leu Pro Tyr Val Ile Tyr Arg Leu Asn Ile Thr Leu Pro

420

430

ccc aca tcc aga ctt gtt tgt gaa ctg agt tgc tat gca att gtt aat 1344

Pro Thr Ser Arg Leu Val Cys Glu Leu Ser Cys Tyr Ala Ile Val Asn

435

440

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ttc ata act ttt tac atc ttt ctg aac aag act ttt cag tgg cca aat 1392
Phe Ile Thr Phe Tyr Ile Phe Leu Asn Lys Thr Phe Gln Trp Pro Asn 450
455
460

agt cag gac att caa agg ttt atg tgg taa tatcagtgat attttgaact 1442 Ser Gln Asp Ile Gln Arg Phe Met Trp 465 470

gtaaaaatgg acttaataat agaccatttc tacaaagaac aactgaatag gnggaaaaca 1502

tggaatttct tttaggtgca gtggtggtct tcaaattaca ttagtttttt taatatatat 1562

tttaaacata tgtaagaaat taagtggcaa agaactggga aagcttaaga cctgcttcaa 1622

angcctgaat aatgggaaaa taaanwngtt tncagatatc tcatatcgct cnnnknatgn 1682

tggcccytmn caangettgg gaatgkttnn wntgnataag ttnattaaan etgggnntge 1742

tnnmwatnac ttnnnkncca nccwnnnwac natgnnntan nnantattta caaaggtcag 1802

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<213> Homo sapiens

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Glu Pro Tyr Met Asp Glu Ile Phe His Leu Pro Gln Ala Gln Arg Tyr 35 40 45

Cys Glu Gly His Phe Ser Leu Ser Gln Trp Asp Pro Met Ile Thr Thr 50 55 60

Leu Pro Gly Leu Tyr Leu Val Ser Val Gly Val Val Lys Pro Ala Ile Trp Ile Phe Gly Trp Ser Glu His Val Val Cys Ser Ile Gly Met Leu Arg Phe Val Asn Leu Leu Phe Ser Val Gly Asn Phe Tyr Leu Leu Tyr Leu Leu Phe His Lys Val Gln Pro Arg Asn Lys Ala Ala Ser Ser Ile Gln Arq Val Leu Ser Thr Leu Thr Leu Ala Val Phe Pro Thr Leu Tyr Phe Phe Asn Phe Leu Tyr Tyr Thr Glu Ala Gly Ser Met Phe Phe Thr Leu Phe Ala Tyr Leu Met Cys Leu Tyr Gly Asn His Lys Thr Ser Ala Phe Leu Gly Phe Cys Gly Phe Met Phe Arg Gln Thr Asn Ile Ile Trp Ala Val Phe Cys Ala Gly Asn Val Ile Ala Gln Lys Leu Thr Glu Ala Trp Lys Thr Glu Leu Gln Lys Lys Glu Asp Arg Leu Pro Pro Ile Lys Gly Pro Phe Ala Glu Phe Arg Lys Ile Leu Gln Phe Leu Leu Ala Tyr Ser Met Ser Phe Lys Asn Leu Ser Met Leu Phe Cys Leu Thr Trp Pro

Tyr Ile Leu Leu Gly Phe Leu Phe Cys Ala Phe Val Val Asn Gly Gly Ile Val Ile Gly Asp Arg Ser Ser His Glu Ala Cys Leu His Phe Pro Gln Leu Phe Tyr Phe Phe Ser Phe Thr Leu Phe Phe Ser Phe Pro His Leu Leu Ser Pro Ser Lys Ile Lys Thr Phe Leu Ser Leu Val Trp Lys His Gly Ile Leu Phe Leu Val Val Thr Leu Val Ser Val Phe Leu Val Trp Lys Phe Thr Tyr Ala His Lys Tyr Leu Leu Ala Asp Asn Arg His Tyr Thr Phe Tyr Val Trp Lys Arg Val Phe Gln Arg Tyr Ala Ile Leu Lys Tyr Leu Leu Val Pro Ala Tyr Ile Phe Ala Gly Trp Ser Ile Ala Asp Ser Leu Lys Ser Lys Pro Ile Phe Trp Asn Leu Met Phe Phe Ile Cys Leu Phe Ile Val Ile Val Pro Gln Lys Leu Leu Glu Phe Arg Tyr Phe Ile Leu Pro Tyr Val Ile Tyr Arg Leu Asn Ile Thr Leu Pro Pro Thr Ser Arg Leu Val Cys Glu Leu Ser Cys Tyr Ala Ile Val Asn

Phe Ile Thr Phe Tyr Ile Phe Leu Asn Lys Thr Phe Gln Trp Pro Asn 450 455 460

Ser Gln Asp Ile Gln Arg Phe Met Trp 465 470

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Asn Ala Arg Val Glu Asn Cys Ala Val Ile Tyr Cys Asn Asp Gly Phe 35 40 45

Cys Glu Leu Cys Gly Tyr Ser Arg Ala Glu Val Met Gln Arg Pro Cys 50 55 60

Thr Cys Asp Phe Leu His Gly Pro Arg Thr Gln Arg Arg Ala Ala Ala 65 70 75 80

Gln Ile Ala Gln Ala Leu Leu Gly Ala Glu Glu Arg Lys Val Glu Ile 85 90 95

Ala Phe Tyr Arg Lys Asp Gly Ser Cys Phe Leu Cys Leu Val Asp Val
100 105 110

Val Pro Val Lys Asn Glu Asp Gly Ala Val Ile Met Phe Ile Leu Asn 115 120 125

Phe Glu Val Val Met Glu Lys Asp Met Val Gly Ser Pro Ala His Asp 130 135 140

Thr Asn His Arg Gly Pro Pro Thr Ser Trp Leu Ala Pro Gly Arg Ala 145 150 155 160

Lys Thr Phe Arg Leu Lys Leu Pro Ala Leu Leu Ala Leu Thr Ala Arg 165 170 175 Glu Ser Ser Val Arg Ser Gly Gly Ala Gly Ala Gly Ala Pro Gly Ala Val Val Asp Val Asp Leu Thr Pro Ala Ala Pro Ser Ser Glu Ser Leu Ala Leu Asp Glu Val Thr Ala Met Asp Asn His Val Ala Gly Leu Gly Pro Ala Glu Glu Arg Arg Ala Leu Val Gly Pro Gly Ser Pro Pro Arg Ser Ala Pro Gly Gln Leu Pro Ser Pro Arg Ala His Ser Leu Asn Pro Asp Ala Ser Gly Ser Ser Cys Ser Leu Ala Arg Thr Arg Ser Arg Glu Ser Cys Ala Ser Val Arg Arg Ala Ser Ser Ala Asp Asp Ile Glu Ala Met Arg Ala Gly Val Leu Pro Pro Pro Pro Arg His Ala Ser Thr Gly Ala Met His Pro Leu Arg Ser Gly Leu Leu Asn Ser Thr Ser Asp Ser Asp Leu Val Arg Tyr Arg Thr Ile Ser Lys Ile Pro Gln Ile Thr Leu Asn Phe Val Asp Leu Lys Gly Asp Pro Phe Leu Ala Ser Pro Thr Ser Asp Arg Glu Ile Ile Ala Pro Lys Ile Lys Glu Arg Thr His Asn Val Thr Glu Lys Val Thr Gln Val Leu Ser Leu Gly Ala Asp Val Leu Pro Glu Tyr Lys Leu Gln Ala Pro Arg Ile His Arg Trp Thr Ile Leu His Tyr Ser Pro Phe Lys Ala Val Trp Asp Trp Leu Ile Leu Leu Leu Val Ile Tyr Thr Ala Val Phe Thr Pro Tyr Ser Ala Ala Phe Leu

Leu Lys Glu Thr Glu Glu Gly Pro Pro Ala Thr Glu Cys Gly Tyr Ala Cys Gln Pro Leu Ala Val Val Asp Leu Ile Val Asp Ile Met Phe Ile Val Asp Ile Leu Ile Asn Phe Arg Thr Thr Tyr Val Asn Ala Asn Glu Glu Val Val Ser His Pro Gly Arg Ile Ala Val His Tyr Phe Lys Gly Trp Phe Leu Ile Asp Met Val Ala Ala Ile Pro Phe Asp Leu Leu Ile Phe Gly Ser Glu Glu Leu Ile Gly Leu Leu Lys Thr Ala Arg Leu Leu Arg Leu Val Arg Val Ala Arg Lys Leu Asp Arg Tyr Ser Glu Tyr Gly Ala Ala Val Leu Phe Leu Leu Met Cys Thr Phe Ala Leu Ile Ala His Trp Leu Ala Cys Ile Trp Tyr Ala Ile Gly Asn Met Glu Gln Pro His Met Asp Ser Arg Ile Gly Trp Leu His Asn Leu Gly Asp Gln Ile Gly Lys Pro Tyr Asn Ser Ser Gly Leu Gly Gly Pro Ser Ile Lys Asp Lys Tyr Val Thr Ala Leu Tyr Phe Thr Phe Ser Ser Leu Thr Ser Val Gly Phe Gly Asn Val Ser Pro Asn Thr Asn Ser Glu Lys Ile Phe Ser Ile Cys Val Met Leu Ile Gly Ser Leu Met Tyr Ala Ser Ile Phe Gly Asn Val Ser Ala Ile Ile Gln Arg Leu Tyr Ser Gly Thr Ala Arg Tyr His Thr Gln Met Leu Arq Val Arq Glu Phe Ile Arq Phe His Gln

Ile Pro Asn Pro Leu Arg Gln Arg Leu Glu Glu Tyr Phe Gln His Ala Trp Ser Tyr Thr Asn Gly Ile Asp Met Asn Ala Val Leu Lys Gly Phe Pro Glu Cys Leu Gln Ala Asp Ile Cys Leu His Leu Asn Arg Ser Leu Leu Gln His Cys Lys Pro Phe Arg Gly Ala Thr Lys Gly Cys Leu Arg Ala Leu Ala Met Lys Phe Lys Thr Thr His Ala Pro Pro Gly Asp Thr Leu Val His Ala Gly Asp Leu Leu Thr Ala Leu Tyr Phe Ile Ser Arg Gly Ser Ile Glu Ile Leu Arg Gly Asp Val Val Ala Ile Leu Gly Lys Asn Asp Ile Phe Gly Glu Pro Leu Asn Leu Tyr Ala Arg Pro Gly Lys Ser Asn Gly Asp Val Arg Ala Leu Thr Tyr Cys Asp Leu His Lys Ile His Arq Asp Asp Leu Leu Glu Val Leu Asp Met Tyr Pro Glu Phe Ser Asp His Phe Trp Ser Ser Leu Glu Ile Thr Phe Asn Leu Arg Asp Thr Asn Met Ile Pro Gly Ser Pro Gly Ser Thr Glu Leu Glu Gly Gly Phe Ser Arg Gln Arg Lys Arg Lys Leu Ser Phe Arg Arg Arg Thr Asp Lys Asp Thr Glu Gln Pro Gly Glu Val Ser Ala Leu Gly Pro Gly Arg Ala Gly Ala Gly Pro Ser Ser Arg Gly Arg Pro Gly Gly Pro Trp Gly Glu Ser Pro Ser Ser Gly Pro Ser Ser Pro Glu Ser Ser Glu Asp Glu

Gly Pro Gly Arg Ser Ser Ser Pro Leu Arg Leu Val Pro Phe Ser Ser 945 950 955 960

Pro Arg Pro Pro Gly Glu Pro Pro Gly Glu Pro Leu Met Glu Asp 965 970 975

Cys Glu Lys Ser Ser Asp Thr Cys Asn Pro Leu Ser Gly Ala Phe Ser 980 985 990

Gly Val Ser Asn Ile Phe Ser Phe Trp Gly Asp Ser Arg Gly Arg Gln 995 1000 1005

Tyr Gln Glu Leu Pro Arg Cys Pro Ala Pro Thr Pro Ser Leu Leu 1010 1015 1020

Asn Ile Pro Leu Ser Ser Pro Gly Arg Arg Pro Arg Gly Asp Val 1025 1030 1035

Glu Ser Arg Leu Asp Ala Leu Gln Arg Gln Leu Asn Arg Leu Glu
1040 1045 1050

Thr Arg Leu Ser Ala Asp Met Ala Thr Val Leu Gln Leu Leu Gln 1055 1060 1065

Arg Gln Met Thr Leu Val Pro Pro Ala Tyr Ser Ala Val Thr Thr 1070 1075 1080

Pro Gly Pro Gly Pro Thr Ser Thr Ser Pro Leu Leu Pro Val Ser 1085 1090 1095

Pro Leu Pro Thr Leu Thr Leu Asp Ser Leu Ser Gln Val Ser Gln 1100 1105 1110

Phe Met Ala Cys Glu Glu Leu Pro Pro Gly Ala Pro Glu Leu Pro 1115 1120 1125

Gln Glu Gly Pro Thr Arg Arg Leu Ser Leu Pro Gly Gln Leu Gly
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Ala Leu Thr Ser Gln Pro Leu His Arg His Gly Ser Asp Pro Gly
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Ser

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<212> DNA

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Met Ser Thr Leu Ser Asn Phe Thr Gln Thr Leu Glu

1 5 10

gac gtc ttc cga agg att ttt att act tat atg gac aat tgg cgc cag 157 Asp Val Phe Arg Arg Ile Phe Ile Thr Tyr Met Asp Asn Trp Arg Gln

15 20 25

aac aca aca get gag caa gag gee ete caa gee aaa gtt gat get gag 205

Asn Thr Thr Ala Glu Gln Glu Ala Leu Gln Ala Lys Val Asp Ala Glu

30 35 40

aac ttc tac tat gtc atc ctg tac ctc atg gtg atg att gga atg ttc
253
Asn Phe Tyr Tyr Val Ile Leu Tyr Leu Met Val Met Ile Gly Met Phe
45
50
55
60

tct ttc atc atc gtg gcc atc ctg gtg agc act gtg aaa tcc aag aga 301 Ser Phe Ile Ile Val Ala Ile Leu Val Ser Thr Val Lys Ser Lys Arg

65 70 75

cgg gaa cac tcc aat gac ccc tac cac cag tac att gta gag gac tgg 349 Arg Glu His Ser Asn Asp Pro Tyr His Gln Tyr Ile Val Glu Asp Trp 80 85 90

cag gaa aag tac aag agc caa atc ttg aat cta gaa gaa tcg aag gcc 397

Gln Glu Lys Tyr Lys Ser Gln Ile Leu Asn Leu Glu Glu Ser Lys Ala

95 100 105

acc atc cat gag aac att ggt gcg gct ggg ttc aaa atg tcc ccc tga 445

Thr Ile His Glu Asn Ile Gly Ala Ala Gly Phe Lys Met Ser Pro

110 115 120

taagggagaa aggcaccaag ctaacatctg acgtccagac atgaagagat gccagtgcca 505

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attttcatgg agattatgtg gttggccaat aaagatagat gacatttcaa tctcagtgat 625

ttatgcttgc ttgttggagc aatattttgt gctgaagacc tcttttactt tccgggcaag 685

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<212> PRT

<213> Homo sapiens

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Glu Gln Glu Ala Leu Gln Ala Lys Val Asp Ala Glu Asn Phe Tyr Tyr 35 40 45

Val Ile Leu Tyr Leu Met Val Met Ile Gly Met Phe Ser Phe Ile Ile 50 55 60

Val Ala Ile Leu Val Ser Thr Val Lys Ser Lys Arg Arg Glu His Ser 65 70 75 80

Asn Asp Pro Tyr His Gln Tyr Ile Val Glu Asp Trp Gln Glu Lys Tyr 85 90 95

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20